Law of Disclaimer

Statements during prosecution of an application "'limit[] the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution.'"

Springs Windows Fashions v. Novo Indus., Inc., 323 F.3d 989, 994 (Fed. Cir. 2003) (citation omitted)

"The doctrine of prosecution disclaimer is well established in Supreme Court precedent, precluding patentees from recapturing through claim interpretation specific meanings disclaimed during prosecution."

Omega Eng'g, Inc. v. Raytek Corp., 334 F.3d 1314, 1323-24 (Fed. Cir. 2003)

"The purpose of consulting the prosecution history is to exclude any interpretation that was disclaimed during prosecution.'"

Chimie v. PPG Industries Inc., 402 F.3d 1371, 1384 (Fed. Cir. 2005)

May 31, 2011 USPTO Office Action

with BDDE. With regard to the amount of uncrosslinked HA being present is greater than 20%, the preferred embodiment shows 6.5% crosslinking and therefore the remaineder (93.5%) would be uncrosslinked. With regard to the degree of crosslinking being about 2%, it would have been obvious to adjust the crosslinking through routine optimization since the instant

regard to the concentration

obvious to one of ordinary s

the instant concentration thr

Claims 1-36 are rejec

Any inquiry concernir

examiner should be directec

9925. The examiner can nc

If attempts to reach t

supervisor, Fereydoun G. S

number for the organization where this application or proceeding is assigned is 571-273-8300.

With regard to the degree of crosslinking being about 2%, it would have been obvious to adjust the crosslinking through routine optimization since the instant amount is within the range taught in the prior art. With regard to the concentration of lidocaine present in the hydrogel it would have been obvious to one of ordinary skill in the art at the time of the instant invention to arrive at the instant concentration through routine optimization.

Source: Ex. 15 to Defendants' Answering Claim Construction Brief – '475 Patent, May 31, 2011 USPTO Office Action, p. 11

2006/0194758 A1, Lebreton

[0081] The procedure remains identical to that of Example 2.

[0082] R=[BDDE]$_0$/[NaHA]$_0$=7%; [NaHA]$_i$=140 mg/g; [NaHA]$_f$=26 mg/g

[0083] Injection force after sterilization: 15 N

[0084] Remanence index of the hydrogel: 3.6

[0085] Monophase hydrogel

EXAMPLE 4

Mixture of Fibers

[0086] The experiment of Example 3 is repeated, modifying the proportions by weight. Proportions by weight in the mixture: 600/2800:90/10 (w/w).

[0087] The procedure is identical to that of Example 2.

[0088] R=[BDDE]$_0$/[NaHA]$_0$=6.5%; [NaHA]$_i$=140 mg/g; [NaHA]$_f$=26 mg/g

[0089] Injection force after sterilization: 14 N

[0090] Remanence index of the hydrogel: 7.7

[0091] Monophase hydrogel

[0092] Said Examples are summarized in the Table below.

TABLE

[NaHA]$_0$ = concentration of NaHA in the reaction medium at t_0
[NaHA]$_f$ = concentration of NaHA in the final hydrogel after reaction and dilution with a sufficient amount of phosphate buffer
G': modulus of elasticity of the final hydrogel (Pa · s)
G": modulus of viscosity of the final hydrogel (Pa · s)
Tan · delta = G"/G'
η_{int} : intrinsic viscosity of the NaHA fiber/Ubbelohde viscometer
F: ejection force of the gel in N through a 27 G½ needle/100 N dynamometer
Carrimed CSL 500 rheometer

n°	η_{int} (ml/g) % = proportion by weight in mixture	R = m_{BDDE}/m_{NaHA}	[NaHA]$_i$ mg/g	[NaHA]$_f$ in final gel mg/g	Appearance*	G', G", tan · delta (1 Hz)	F_{sp} 27 G½
1	(100%) 2800	6%	105	26	M	143/65/0.40	25
2	(100%) 600	6.8%	174	26	B	1300/100/0.08	24
3	(77%) 600 + (23%) 2800	7	140	26	M	262/27/0.10	15
4	(90%) 600 + (10%) 2800	6.5	140	26	M	571/41/0.07	14

*M = monophase
B = biphase

[0093] The attached FIGURE shows the following curve:

Tan .delta=f (stressing frequency)

for each of the four hydrogels prepared according to Examples 1 to 4.

[0094] The rheological behavior of the hydrogels of the invention (Examples 3 and 4) is different from that of the hydrogel of the prior art (Example 1).

[0095] Furthermore, the hydrogels of the invention are monophase and thus very different from the hydrogel of Example 2 (biphase).

1. Process for the crosslinking of at least one polymer selected from polysaccharides and derivatives thereof, which is carried out in an aqueous solvent by the action of an effective and non-excessive amount of at least one crosslinking agent, characterized in that it is carried out on a mixture containing at least one low-molecular weight polymer and at least one high-molecular weight polymer.

2. Process according to claim 1, characterized in that said mixture contains a single polymer with at least two different molecular weights, at least one being low and at least one being high, and advantageously with two different mol… weights, one low and one high.

3. Process according to … said polymer is a hyalur…

4. Process according to … hyaluronic acid salt is s… potassium salt and mixt… consists of the sodium sa…

5. Process according t… acterized in that said mix…

at least one hyaluronic … m, where m≦9.9 … Da≦m≦9.9.10^5 Da;

at least one hyaluronic … M, where M≧10^6 Da … Da, and very adva… Da,

said low-molecular w… salts advantageously … advantageously cons…

6. Process according to … mixture has an intrinsic …

7. Process according to … said mixture contains mo… geously more than 70% by … acid salt of low molecula… weight, advantageously h… one hyaluronic acid salt …

8. Process according t… acterized in that said mixt… of at least one high-molec…

9. Process according t… acterized in that said mixt… of the sodium salt of hy… weight of about 3.10^5 Da … sodium salt of hyaluronic … about 3.10^6 Da.

EXAMPLE 4

Mixture of Fibers

[0086] The experiment of Example 3 is repeated, modifying the proportions by weight. Proportions by weight in the mixture: 600/2800:90/10 (w/w).

[0087] The procedure is identical to that of Example 2.

[0088] R=[BDDE]$_0$/[NaHA]$_0$=6.5%; [NaHA]$_i$=140 mg/g; [NaHA]$_f$=26 mg/g

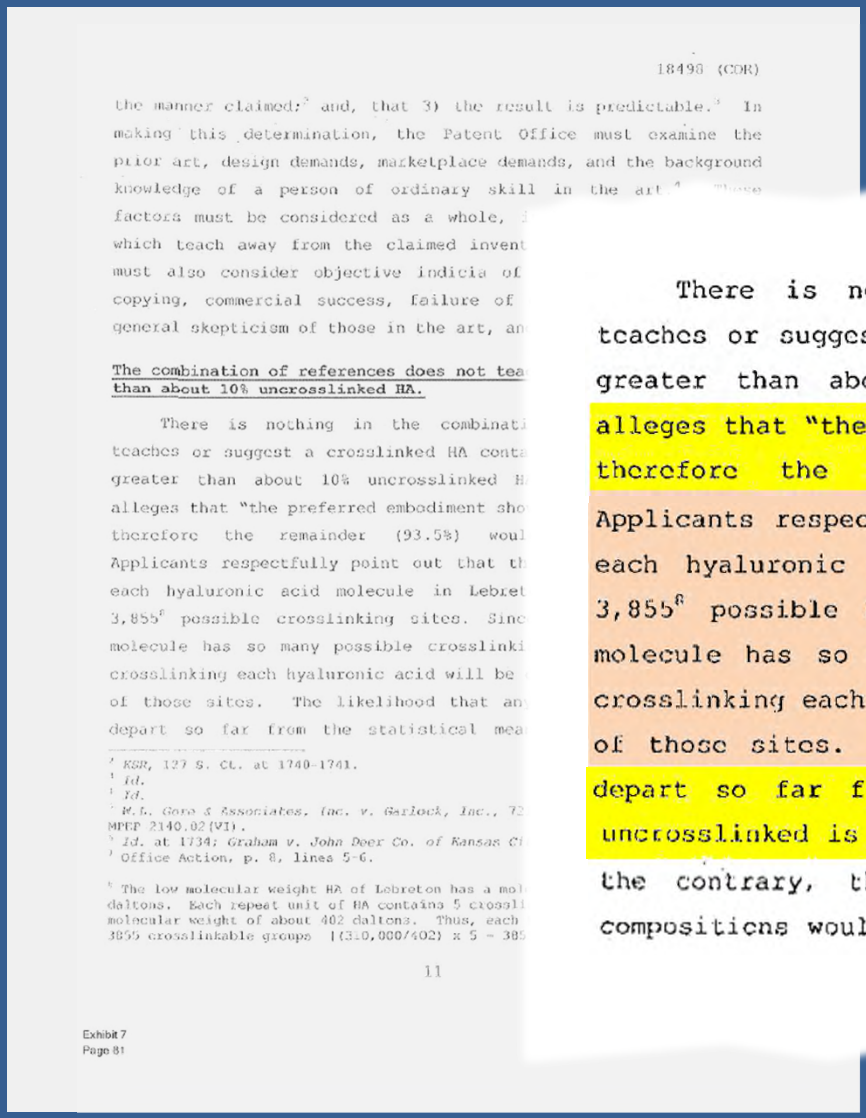
[0089] Injection force after sterilization: 14 N

[0090] Remanence index of the hydrogel: 7.7

[0091] Monophase hydrogel

Source: 2006/0194758, [0086]-[0091]

November 9, 2011 Response to Office Action



18498 (CDR)

the manner claimed;[2] and, that 3) the result is predictable.[3] In making this determination, the Patent Office must examine the prior art, design demands, marketplace demands, and the background knowledge of a person of ordinary skill in the art.[4] Those factors must be considered as a whole, which teach away from the claimed invent must also consider objective indicia of copying, commercial success, failure of general skepticism of those in the art, an

The combination of references does not tea than about 10% uncrosslinked HA.

There is nothing in the combinati teaches or suggest a crosslinked HA cont greater than about 10% uncrosslinked H alleges that "the preferred embodiment sho therefore the remainder (93.5%) woul Applicants respectfully point out that th each hyaluronic acid molecule in Lebret 3,855[6] possible crosslinking sites. Sinc molecule has so many possible crosslinki crosslinking each hyaluronic acid will be of those sites. The likelihood that an depart so far from the statistical mea

[2] *KSR*, 127 S. Ct. at 1740-1741.
[3] *Id.*
[4] *Id.*
[5] *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 72 MPEP 2140.02(VI).
[6] *Id.* at 1734; *Graham v. John Deer Co. of Kansas Ci*
[7] Office Action, p. 8, lines 5-6.

[6] The low molecular weight HA of Lebreton has a mol daltons. Each repeat unit of HA contains 5 crossli molecular weight of about 402 daltons. Thus, each 3855 crosslinkable groups [(310,000/402) x 5 = 385

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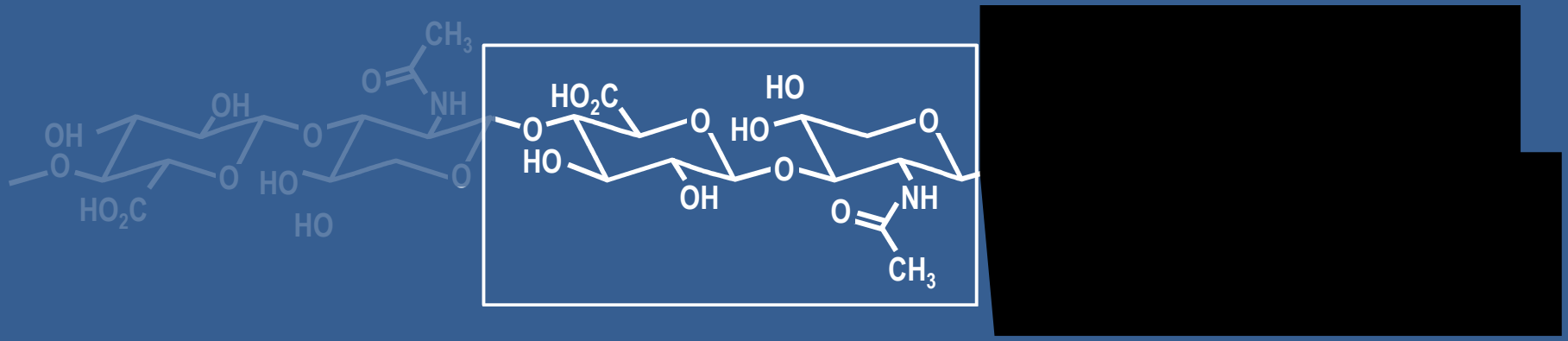
Exhibit 7
Page 81

There is nothing in the combination of references that teaches or suggest a crosslinked HA containing an anesthetic and greater than about 10% uncrosslinked HA. The Office action alleges that "the preferred embodiment shows 6.5% crosslinking and therefore the remainder (93.5%) would be uncrosslinked."[7] Applicants respectfully point out that this is incorrect because each hyaluronic acid molecule in Lebreton has at least about 3,855[6] possible crosslinking sites. Since each hyaluronic acid molecule has so many possible crosslinking sites, even at 6.5% crosslinking each hyaluronic acid will be crosslinked at about 250 of those sites. The likelihood that any hyaluronic acid would depart so far from the statistical mean of 250 so as to be uncrosslinked is infinitesimally small. Thus, absent evidence to the contrary, there is no reason to believe that Lebreton's compositions would have any uncrosslinked HA. Furthermore, there

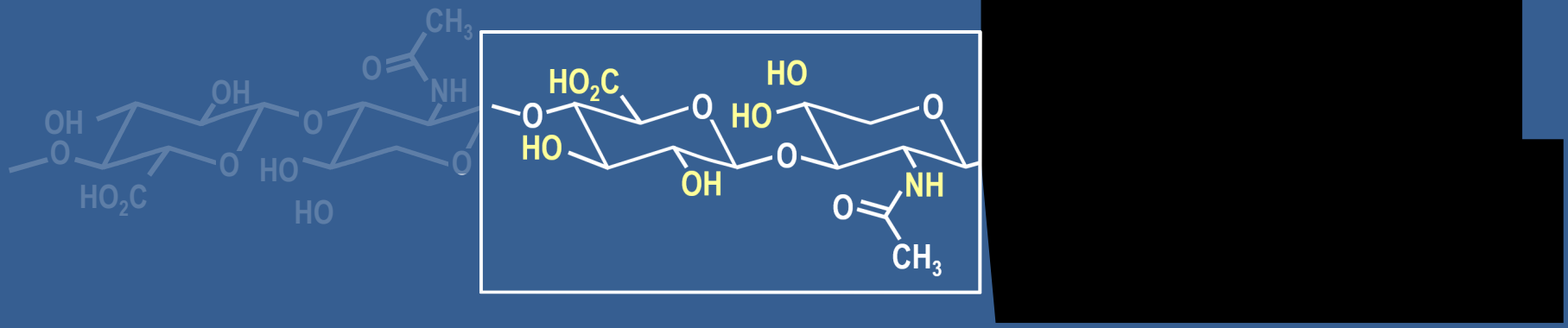
Source: Ex. 7 to Defendants' Opening Claim Construction Brief – '475 Patent, Nov. 9, 2011 Response to Office Action, p. 11

Crosslinking Sites



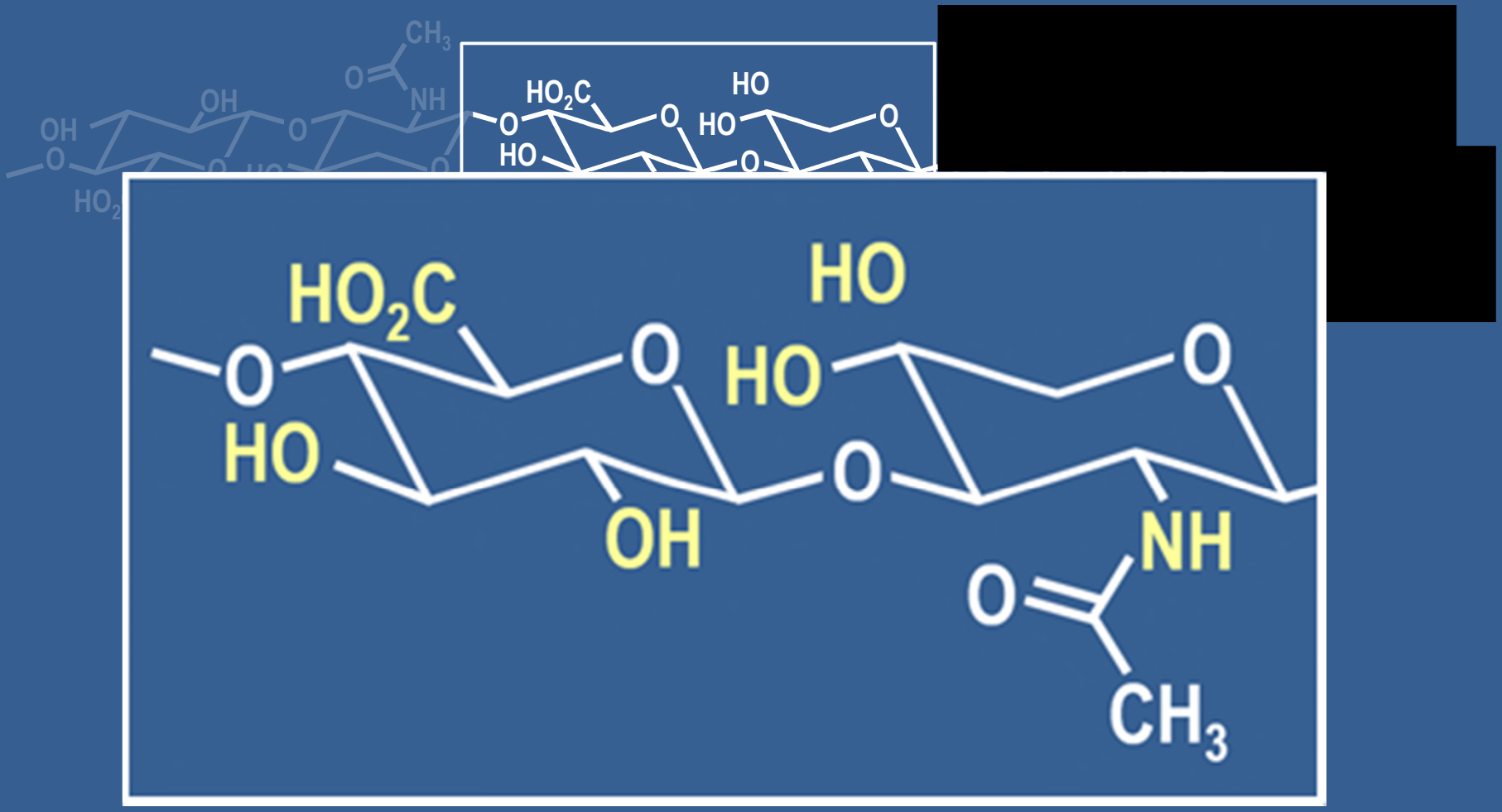
[redacted]

Crosslinking Sites

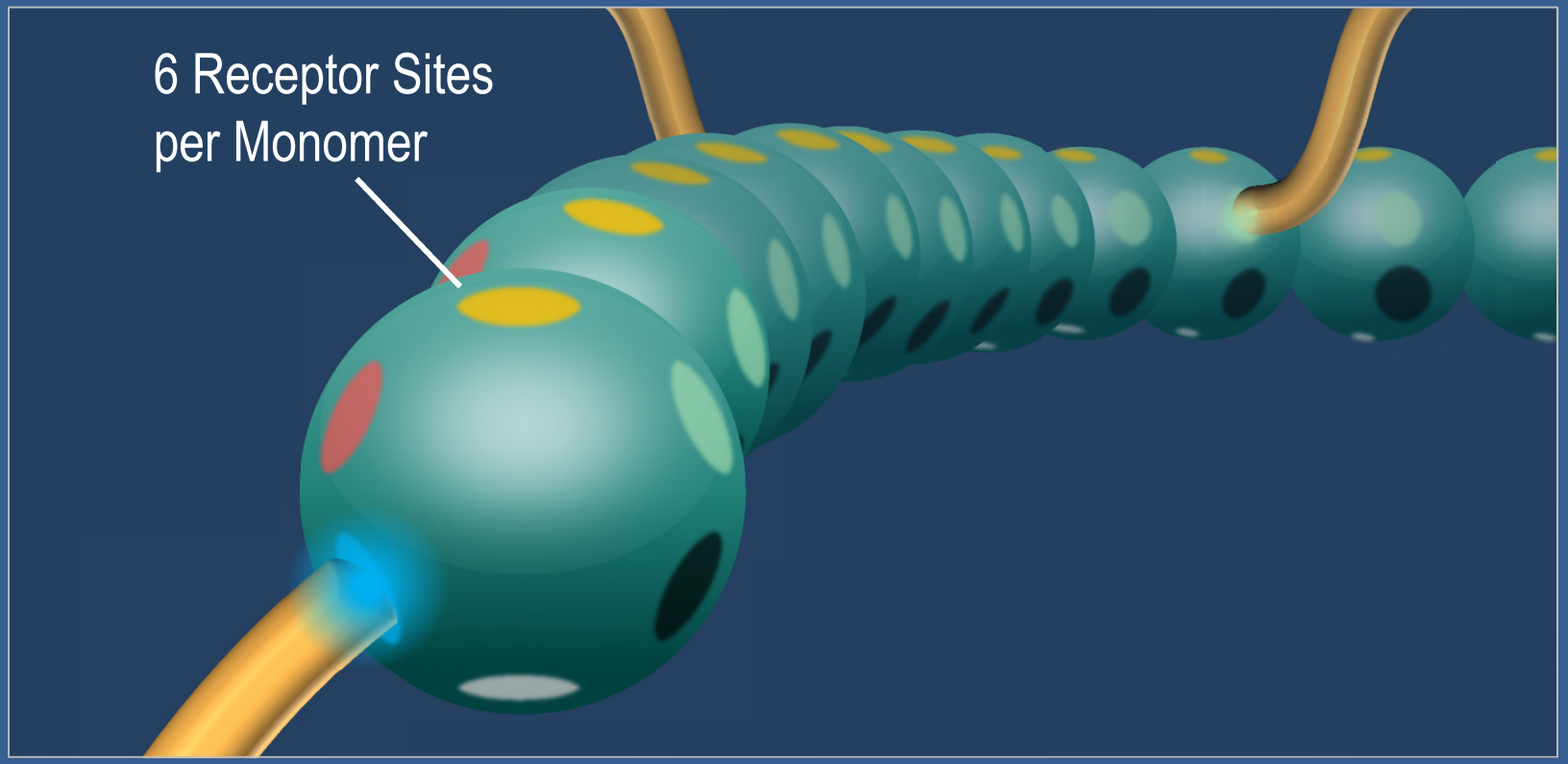


[redacted]

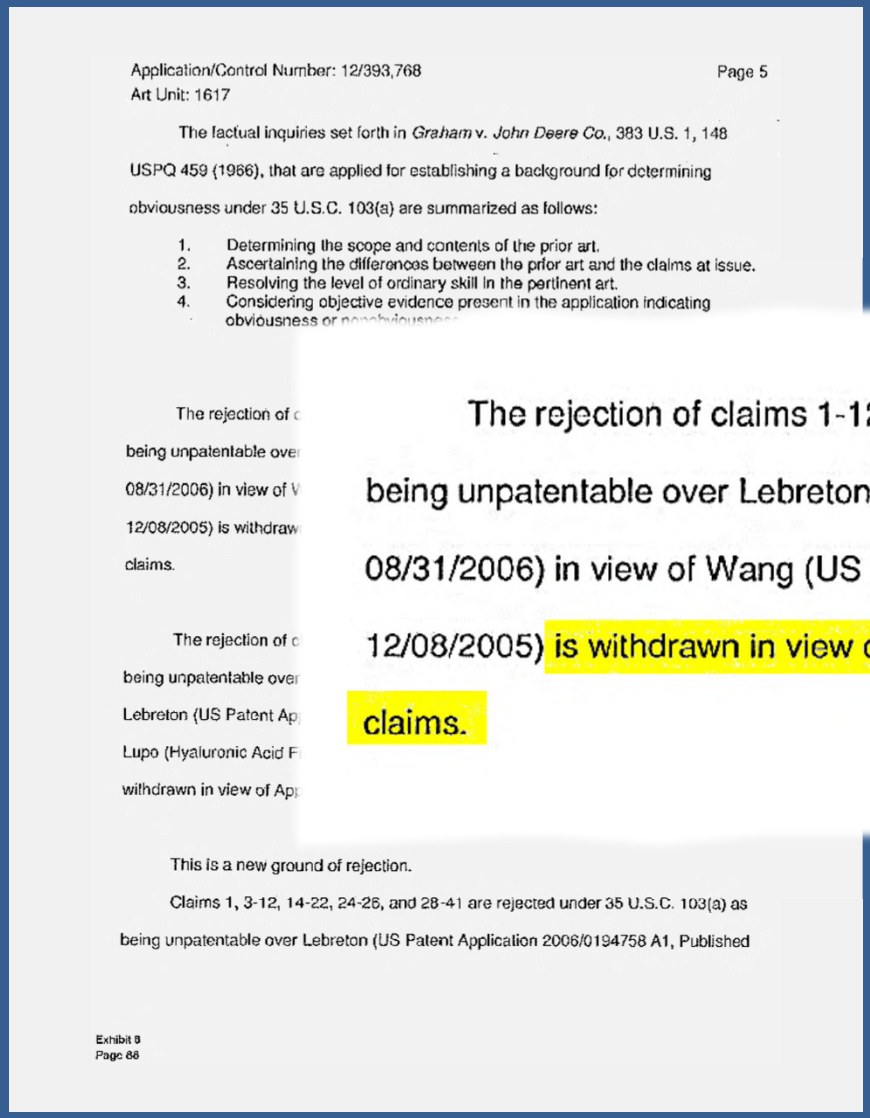
Crosslinking Sites



Crosslinking Sites



January 30, 2012 USPTO Office Action



Application/Control Number: 12/393,768 Page 5
Art Unit: 1617

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or

The rejection of c
being unpatentable ove
08/31/2006) in view of V
12/08/2005) is withdraw
claims.

The rejection of c
being unpatentable over
Lebreton (US Patent Ap
Lupo (Hyaluronic Acid F
withdrawn in view of Ap

This is a new ground of rejection.

Claims 1, 3-12, 14-22, 24-26, and 28-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lebreton (US Patent Application 2006/0194758 A1, Published

Exhibit 8
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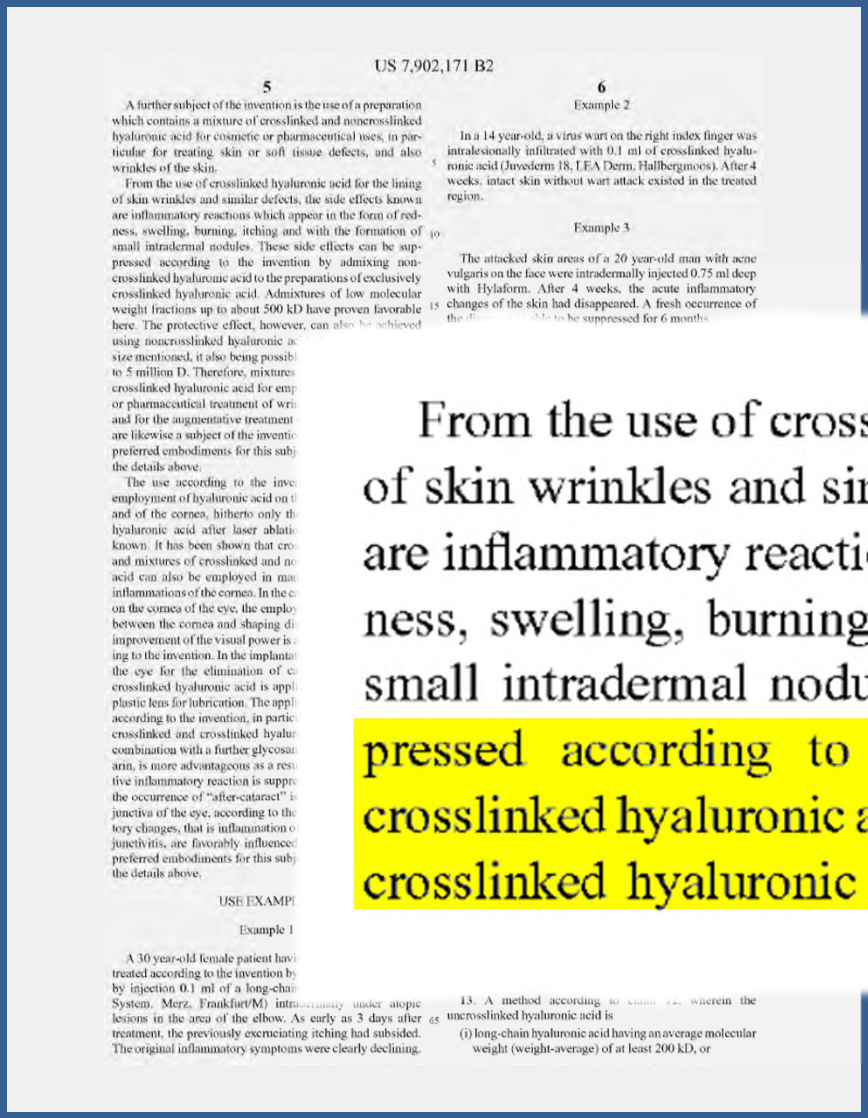
The rejection of claims 1-12, 14-22, 24, and 26-36 under 35 U.S.C. 103(a) as being unpatentable over Lebreton (US Patent Application 2006/0194758 A1, Published 08/31/2006) in view of Wang (US Patent Application 2005/0271729 A1, Published 12/08/2005) is withdrawn in view of Applicant's arguments and amendments to the claims.

Source: Ex. 8 to Defendants' Opening Claim Construction Brief – '475 Patent, Jan. 30, 2012 USPTO Office Action, p. 5

7,902,171 B2 Patent, Reinmuller



US 7,902,171 B2

5

A further subject of the invention is the use of a preparation which contains a mixture of crosslinked and noncrosslinked hyaluronic acid for cosmetic or pharmaceutical uses, in particular for treating skin or soft tissue defects, and also wrinkles of the skin.

From the use of crosslinked hyaluronic acid for the lining of skin wrinkles and similar defects, the side effects known are inflammatory reactions which appear in the form of redness, swelling, burning, itching and with the formation of small intradermal nodules. These side effects can be suppressed according to the invention by admixing non-crosslinked hyaluronic acid to the preparations of exclusively crosslinked hyaluronic acid. Admixtures of low molecular weight fractions up to about 500 kD have proven favorable here. The protective effect, however, can also be achieved using noncrosslinked hyaluronic ac
size mentioned, it also being possibl
to 5 million D. Therefore, mixtures
crosslinked hyaluronic acid for emp
or pharmaceutical treatment of wri
and for the augmentative treatment
are likewise a subject of the inventio
preferred embodiments for this subj
the details above.

The use according to the inve
employment of hyaluronic acid on t
and of the cornea, hitherto only th
hyaluronic acid after laser ablatio
known. It has been shown that cro
and mixtures of crosslinked and no
acid can also be employed in ma
inflammations of the cornea. In the c
on the cornea of the eye, the employ
between the cornea and shaping di
improvement of the visual power is
ing to the invention. In the implanta
the eye for the elimination of c
crosslinked hyaluronic acid is appl
plastic lens for lubrication. The appl
according to the invention, in partic
crosslinked and crosslinked hyalur
combination with a further glycosa
arin, is more advantageous as a res
tive inflammatory reaction is suppr
the occurrence of "after-cataract" i
junctiva of the eye, according to th
tory changes, that is inflammation o
junctivitis, are favorably influenced
preferred embodiments for this subj
the details above.

USE EXAMPL

Example 1

A 30 year-old female patient havi
treated according to the invention by
by injection 0.1 ml of a long-chai
System, Merz, Frankfurt/M) intra
lesions in the area of the elbow. As early as 3 days after
treatment, the previously excruciating itching had subsided.
The original inflammatory symptoms were clearly declining.

6

Example 2

In a 14 year-old, a virus wart on the right index finger was intralesionally infiltrated with 0.1 ml of crosslinked hyaluronic acid (Juvederm 18, I.E.A Derm, Hallbergmoos). After 4 weeks, intact skin without wart attack existed in the treated region.

Example 3

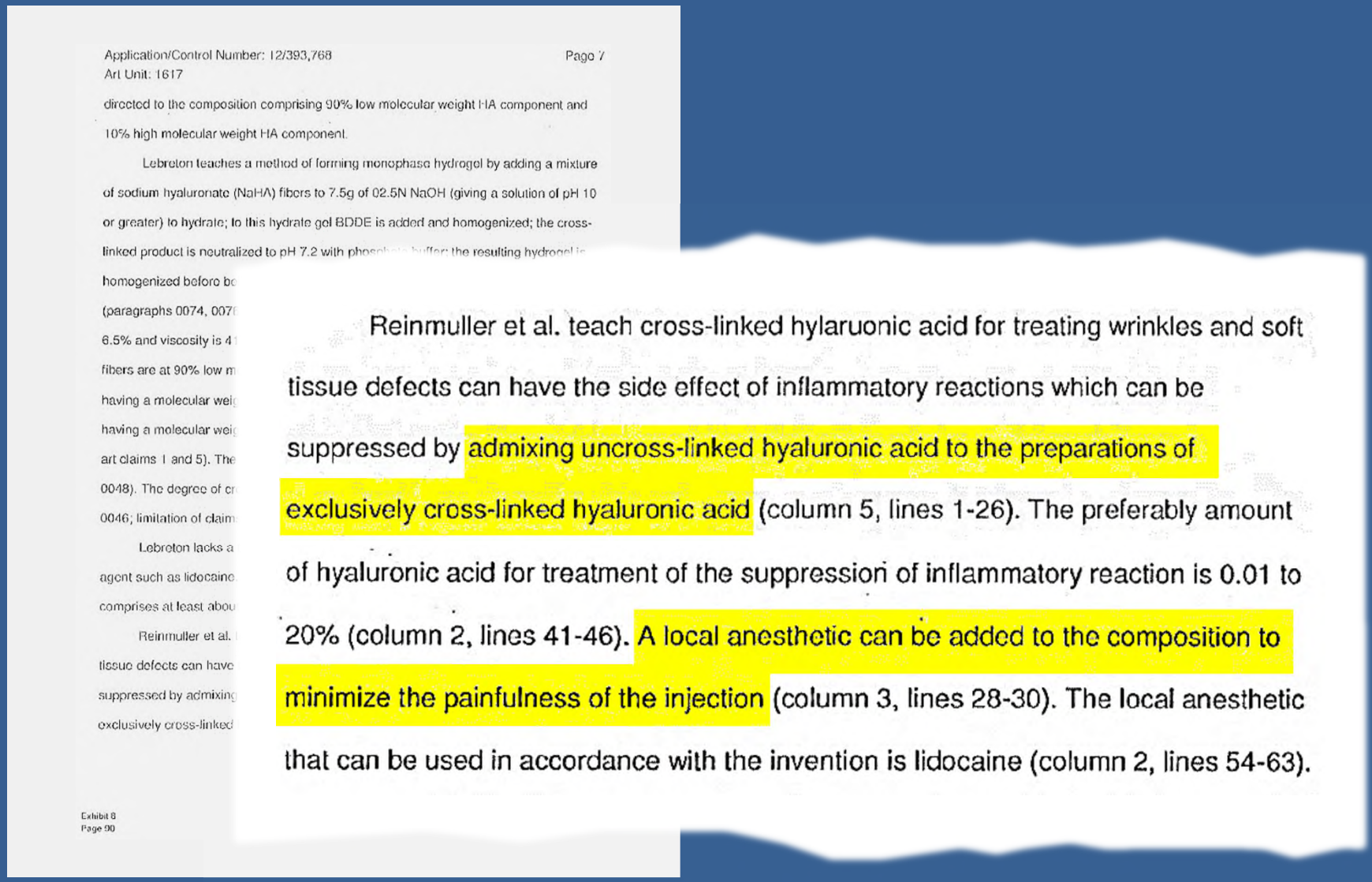
The attacked skin areas of a 20 year-old man with acne vulgaris on the face were intradermally injected 0.75 ml deep with Hylaform. After 4 weeks, the acute inflammatory changes of the skin had disappeared. A fresh occurrence of the
to be suppressed for 6 months

13. A method according to
uncrosslinked hyaluronic acid is
(i) long-chain hyaluronic acid having an average molecular weight (weight-average) of at least 200 kD, or

From the use of crosslinked hyaluronic acid for the lining of skin wrinkles and similar defects, the side effects known are inflammatory reactions which appear in the form of redness, swelling, burning, itching and with the formation of small intradermal nodules. These side effects can be suppressed according to the invention by admixing non-crosslinked hyaluronic acid to the preparations of exclusively crosslinked hyaluronic acid. Admixtures of low molecular

Source: '171 patent, 5:6-13

January 30, 2012 USPTO Office Action



Application/Control Number: 12/393,768 Page 7
Art Unit: 1617

directed to the composition comprising 90% low molecular weight HA component and 10% high molecular weight HA component.

Lebreton teaches a method of forming monophase hydrogel by adding a mixture of sodium hyaluronate (NaHA) fibers to 7.5g of 02.5N NaOH (giving a solution of pH 10 or greater) to hydrate; to this hydrate gel BDDE is added and homogenized; the cross-linked product is neutralized to pH 7.2 with phosphate buffer; the resulting hydrogel is homogenized before bo
(paragraphs 0074, 007
6.5% and viscosity is 4
fibers are at 90% low m
having a molecular wei
having a molecular wei
art claims 1 and 5). The
0048). The degree of cr
0046; limitation of claim

Lebreton lacks a
agent such as lidocaine
comprises at least abou

Reinmuller et al.
tissue defects can have
suppressed by admixing
exclusively cross-linked

Reinmuller et al. teach cross-linked hylaruonic acid for treating wrinkles and soft tissue defects can have the side effect of inflammatory reactions which can be suppressed by admixing uncross-linked hyaluronic acid to the preparations of exclusively cross-linked hyaluronic acid (column 5, lines 1-26). The preferably amount of hyaluronic acid for treatment of the suppression of inflammatory reaction is 0.01 to 20% (column 2, lines 41-46). A local anesthetic can be added to the composition to minimize the painfulness of the injection (column 3, lines 28-30). The local anesthetic that can be used in accordance with the invention is lidocaine (column 2, lines 54-63).

Exhibit 8
Page 90

Source: Ex. 8 to Defendants' Opening Claim Construction Brief – '475 Patent, Jan. 30, 2012 USPTO Office Action, p. 7

January 30, 2012 USPTO Office Action

of hyaluronic acid for treatment of the suppression of inflammatory reaction is 0.01 to 20% (column 2, lines 41-46). A local anesthetic can be added to the composition to minimize the painfulness of the injection [illegible] that can be used in accordance wit[illegible]

It would have been prima fac[illegible] of the instant invention to combine t[illegible] have a reasonable expectation of s[illegible] uncross-linked hyaluronic acid and [illegible] in order to treat inflammation assoc[illegible] also to treat any pain associated wit[illegible] regard to the concentration of lidoc[illegible] obvious to one of ordinary skill in th[illegible] the instant concentration through ro[illegible]

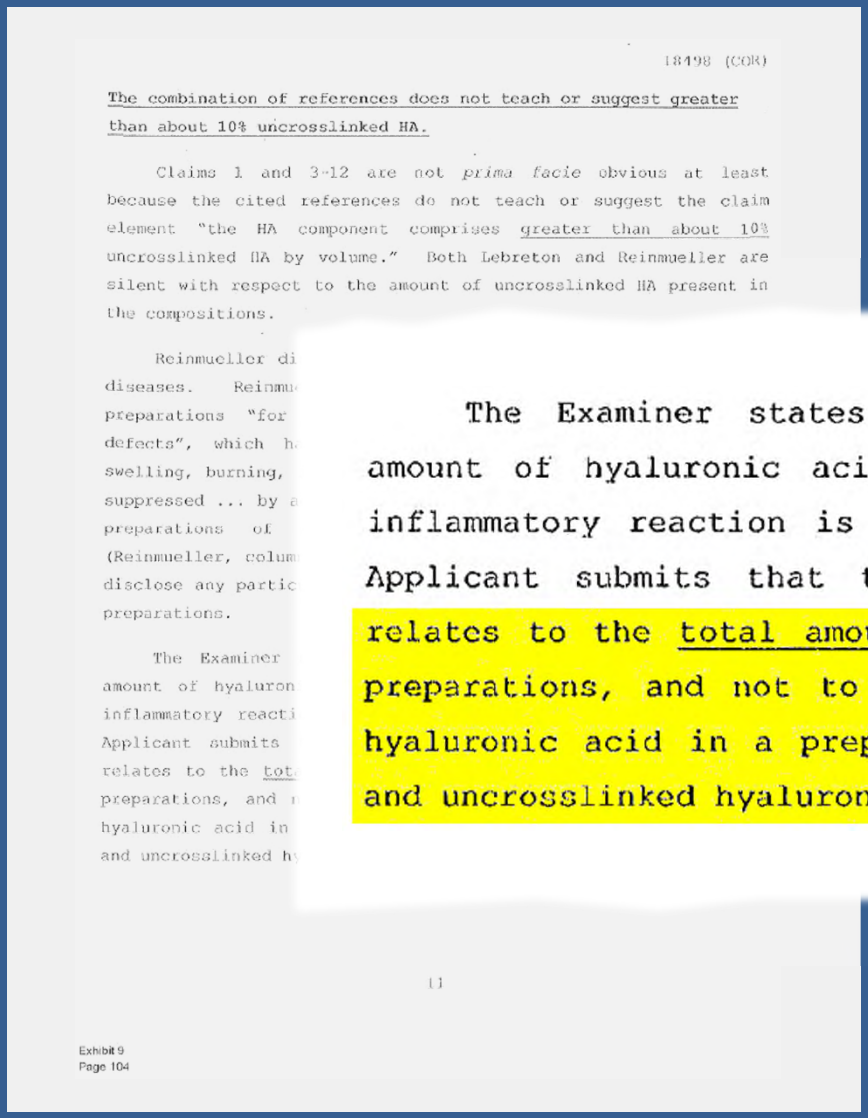
Any inquiry concerning this c[illegible] examiner should be directed to ALI[illegible] 9925. The examiner can normally b[illegible]

If attempts to reach the exam[illegible] supervisor, Fereydoun G. Sajjadi ca[illegible] number for the organization where t[illegible] 273-8300.

It would have been prima facie obvious to one of ordinary skill in the art the time of the instant invention to combine the teachings of Lebreton and Reinmuller et al. and have a reasonable expectation of success. One would have been motivated to add uncross-linked hyaluronic acid and lidocaine to monophase hyaluronic acid of Leberton in order to treat inflammation associated with administration of the soft tissue filler and also to treat any pain associated with the injection of the gel into the soft tissue. With regard to the concentration of lidocaine present in the hydrogel it would have been obvious to one of ordinary skill in the art at the time of the instant invention to arrive at the instant concentration through routine optimization.

Source: Ex. 8 to Defendants' Opening Claim Construction Brief – '475 Patent, Jan. 30, 2012 USPTO Office Action, p. 8

July 30, 2012 Response to Office Action



18498 (COR)

The combination of references does not teach or suggest greater than about 10% uncrosslinked HA.

Claims 1 and 3-12 are not *prima facie* obvious at least because the cited references do not teach or suggest the claim element "the HA component comprises greater than about 10% uncrosslinked HA by volume." Both Lebreton and Reinmueller are silent with respect to the amount of uncrosslinked HA present in the compositions.

Reinmueller di
diseases. Reinmu
preparations "for
defects", which h
swelling, burning,
suppressed ... by a
preparations of
(Reinmueller, colum
disclose any partic
preparations.

The Examiner
amount of hyaluron
inflammatory reacti
Applicant submits
relates to the tot
preparations, and
hyaluronic acid in
and uncrosslinked h

The Examiner states that in Reinmueller, "the preferable amount of hyaluronic acid for treatment of the suppression of inflammatory reaction is 0.01 to 20% (column 2, lines 41-46)". Applicant submits that this specific disclosure in Reinmuller relates to the total amount of hyaluronic acid in Reinmueller's preparations, and not to any percentage amount of uncrosslinked hyaluronic acid in a preparations comprising admixed crosslinked and uncrosslinked hyaluronic acid.

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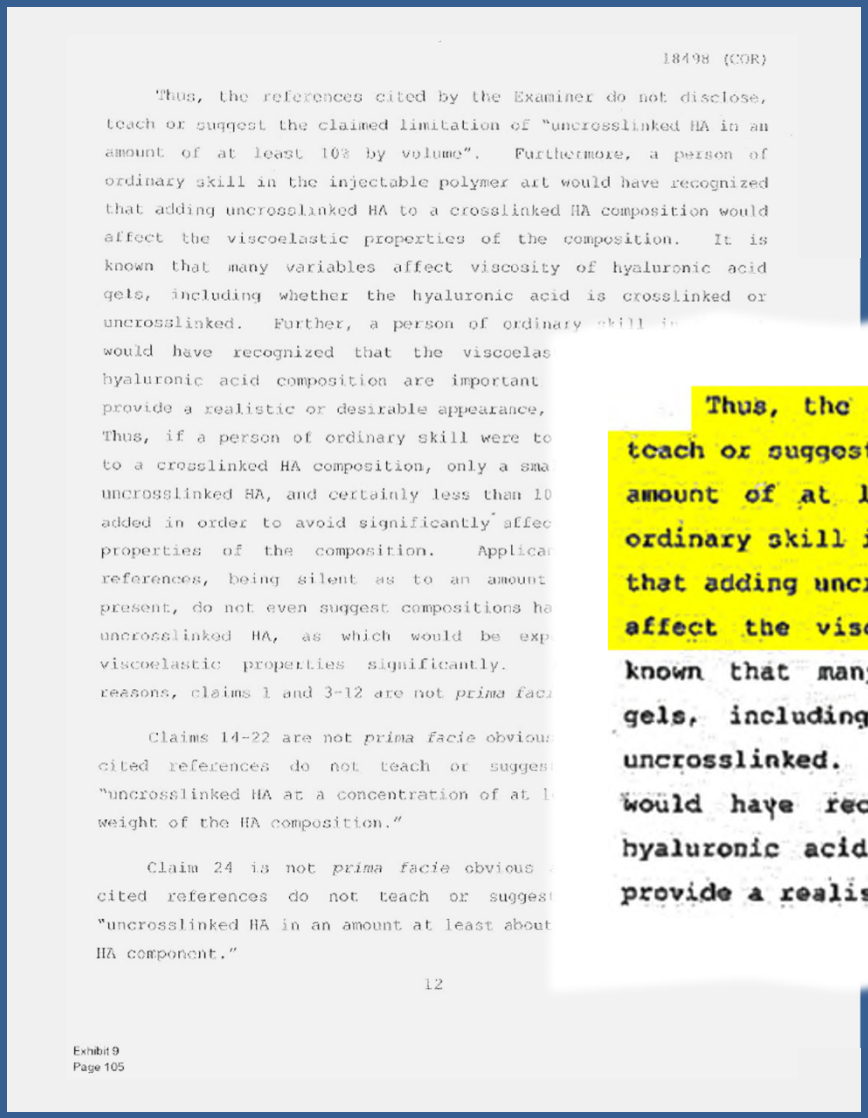
Exhibit 9
Page 104

Source: Ex. 9 to Defendants' Opening Claim Construction Brief – '475 Patent, Jul. 30, 2012 Response to Office Action, p. 11

July 30, 2012 Response to Office Action



18498 (COR)

Thus, the references cited by the Examiner do not disclose, teach or suggest the claimed limitation of "uncrosslinked HA in an amount of at least 10% by volume". Furthermore, a person of ordinary skill in the injectable polymer art would have recognized that adding uncrosslinked HA to a crosslinked HA composition would affect the viscoelastic properties of the composition. It is known that many variables affect viscosity of hyaluronic acid gels, including whether the hyaluronic acid is crosslinked or uncrosslinked. Further, a person of ordinary skill in

would have recognized that the viscoelas
hyaluronic acid composition are important
provide a realistic or desirable appearance,
Thus, if a person of ordinary skill were to
to a crosslinked HA composition, only a sma
uncrosslinked HA, and certainly less than 10
added in order to avoid significantly affec
properties of the composition. Applica
references, being silent as to an amount
present, do not even suggest compositions ha
uncrosslinked HA, as which would be exp
viscoelastic properties significantly.
reasons, claims 1 and 3-12 are not *prima fac*

Claims 14-22 are not *prima facie* obvious
cited references do not teach or sugges
"uncrosslinked HA at a concentration of at l
weight of the HA composition."

Claim 24 is not *prima facie* obvious
cited references do not teach or sugges
"uncrosslinked HA in an amount at least about
HA component."

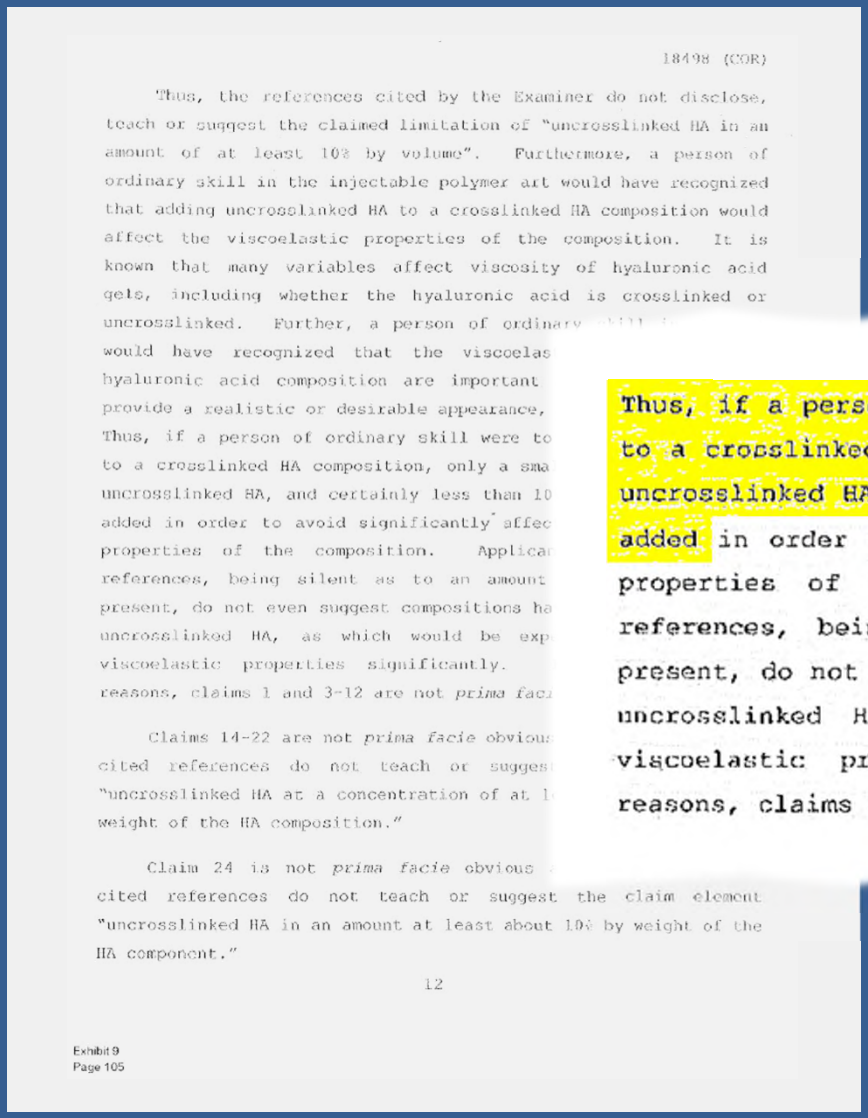
12

Exhibit 9
Page 105

Thus, the references cited by the Examiner do not disclose, teach or suggest the claimed limitation of "uncrosslinked HA in an amount of at least 10% by volume". Furthermore, a person of ordinary skill in the injectable polymer art would have recognized that adding uncrosslinked HA to a crosslinked HA composition would affect the viscoelastic properties of the composition. It is known that many variables affect viscosity of hyaluronic acid gels, including whether the hyaluronic acid is crosslinked or uncrosslinked. Further, a person of ordinary skill in the art would have recognized that the viscoelastic properties of a hyaluronic acid composition are important to help a filler to provide a realistic or desirable appearance, feel, and longevity.

Source: Ex. 9 to Defendants' Opening Claim Construction Brief – '475 Patent, Jul. 30, 2012 Response to Office Action, p. 12

July 30, 2012 Response to Office Action



18498 (COR)

Thus, the references cited by the Examiner do not disclose, teach or suggest the claimed limitation of "uncrosslinked HA in an amount of at least 10% by volume". Furthermore, a person of ordinary skill in the injectable polymer art would have recognized that adding uncrosslinked HA to a crosslinked HA composition would affect the viscoelastic properties of the composition. It is known that many variables affect viscosity of hyaluronic acid gels, including whether the hyaluronic acid is crosslinked or uncrosslinked. Further, a person of ordinary skill in the art would have recognized that the viscoelas hyaluronic acid composition are important provide a realistic or desirable appearance, Thus, if a person of ordinary skill were to to a crosslinked HA composition, only a sma uncrosslinked HA, and certainly less than 10 added in order to avoid significantly affec properties of the composition. Applica references, being silent as to an amount present, do not even suggest compositions ha uncrosslinked HA, as which would be exp viscoelastic properties significantly. reasons, claims 1 and 3-12 are not *prima faci*

Claims 14-22 are not *prima facie* obvious cited references do not teach or sugges "uncrosslinked HA at a concentration of at l weight of the HA composition."

Claim 24 is not *prima facie* obvious cited references do not teach or suggest the claim element "uncrosslinked HA in an amount at least about 10% by weight of the HA component."

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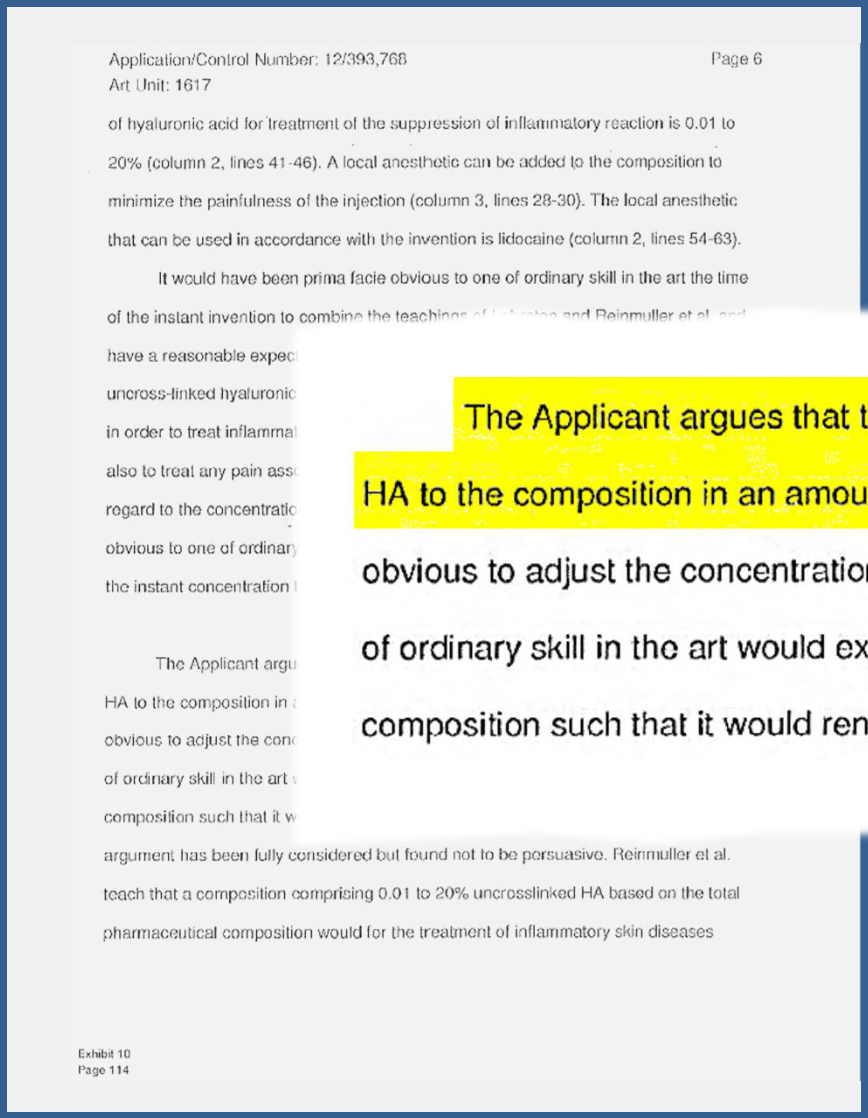
Exhibit 9
Page 105

Thus, if a person of ordinary skill were to add uncrosslinked HA to a crosslinked HA composition, only a small or minor amount of uncrosslinked HA, and certainly less than 10% by volume, would be added in order to avoid significantly affecting the viscoelastic properties of the composition. Applicant submits that the references, being silent as to an amount of uncrosslinked HA present, do not even suggest compositions having greater than 10% uncrosslinked HA, as which would be expected to affect the viscoelastic properties significantly. For at least these reasons, claims 1 and 3-12 are not *prima facie* obvious.

Source: Ex. 9 to Defendants' Opening Claim Construction Brief – '475 Patent, Jul. 30, 2012 Response to Office Action, p. 12

November 19, 2012 USPTO Office Action



Application/Control Number: 12/393,768 Page 6
Art Unit: 1617

of hyaluronic acid for treatment of the suppression of inflammatory reaction is 0.01 to 20% (column 2, lines 41-46). A local anesthetic can be added to the composition to minimize the painfulness of the injection (column 3, lines 28-30). The local anesthetic that can be used in accordance with the invention is lidocaine (column 2, lines 54-63).

It would have been prima facie obvious to one of ordinary skill in the art the time of the instant invention to combine the teachings of [illegible] and Reinmuller et al. and have a reasonable expec[illegible] uncross-linked hyaluronic[illegible] in order to treat inflammat[illegible] also to treat any pain ass[illegible] regard to the concentratio[illegible] obvious to one of ordinary[illegible] the instant concentration[illegible]

The Applicant argu[illegible] HA to the composition in [illegible] obvious to adjust the conc[illegible] of ordinary skill in the art [illegible] composition such that it w[illegible] argument has been fully considered but found not to be persuasive. Reinmuller et al. teach that a composition comprising 0.01 to 20% uncrosslinked HA based on the total pharmaceutical composition would for the treatment of inflammatory skin diseases

Exhibit 10
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The Applicant argues that the prior art does not teach adding the uncrosslinked HA to the composition in an amount of at least 10% and that it would not have been obvious to adjust the concentration to the instantly claimed concentration since this one of ordinary skill in the art would expect that it would change the viscosity of the composition such that it would render it not useful for its intended purpose. Applicant's

Source: Ex. 10 to Defendants' Opening Claim Construction Brief – '475 Patent, Nov. 19, 2012 USPTO Office Action, p. 6